Study of serum Zinc levels in patients with vitiligo of north Telangana

B Venugopal[1], H Kishan Reddy[2].

[1]Assistant Professor, [2]Associate Professor, Department of Biochemistry, Prathima Institute of Medical Sciences, Nagunur, Karimnagar, Telangana, India.

Address for correspondence: Dr. H. Kishan Reddy, Associate Professor, Department of Biochemistry, Prathima Institute of Medical Sciences, Nagunur, Karimnagar, Telangana, India.

Email: drhkr82@gmail.com

ABSTRACT

Introduction:

Vitiligo is an acquired,idiopathic depigmenting skin disorder characterized by circumscribed depigmented macules and patches, which affects approximately 0.1–2% of the general population worldwide. Zinc is an essential trace element that is necessary for growth and development at all stages of life. Some studies have reported an association between serum zinc levels and vitiligo.

Aims :

To measure the serum zinc levels in patients with vitiligo compared to healthy subjects.

Materials & Methods:

35 patients with vitiligo and 35 healthy individual, who were visited various hospitals in Karimnagar, Telangana state taken as cases and controls respectively .The two groups were matched for age and sex. Commercially available Coral kit was used to measure serum zinc levels on CPC-semi auto analyser . The statistical analysis was performed using GRAPHPAD-6 software.

Results: The mean serum level of zinc in vitiligo patients and controls was 35.54 ±11.10 µg/dl, 81.29 ±11.32 µg/dl respectively. The serum zinc level in patients with vitiligo was significantly lower than in healthy controls(p = <0.0001*).

Conclusion: The results of our study revealed a significant association between vitiligo and serum zinc levels.A relative decrease in the serum zinc levels in vitiligo patients can highlight the role of zinc in the pathogenesis of vitiligo.

Keywords: Vitiligo,melanogenesis, serum zinc level.

INTRODUCTION

Vitiligo is a common dermatological disorder characterized by acquired, idiopathic, progressive, circumscribed hypomelanosis of the skin and hair, with total absence of melanocytes microscopically.[1] Various physiological, biochemical, histochemical and enzymatic studies have been done to find out the cause of the disease.[2] Genes certainly play a role in all aspects of vitiligo pathogenesis, even response to environmental triggers, and so genetics really should not be separated out as a distinct phenomenon. [3,4] In the past few years, studies of the genetic epidemiology of generalized vitiligo have led to the recognition that vitiligo is part of a broader, genetically determined, autoimmune, and auto inflammatory diathesis.[3,5] The pathogenesis of this disorder is uncertain, but it appears to be dependent on the interaction of genetic, immunological, and neurological factors [5]. The melanocytes in vitiligo are degenerated and seem to be replaced by Langerhans cells[5].

The linkage signals on chromosomes 1, 7, and 17 in Caucasian families with generalized vitiligo and associated autoimmune diseases have been reported[5]. Some of the suggested pathogeneses include impaired melanocyte migration and/or proliferation, accumulation of toxic compounds[5], infections, and psychological, neural, autoimmune, and autocytotoxic factors [5].

The facts that vitiligo is found more frequently in patients with metastatic melanoma and is associated with an improved prognosis, that vitiligo-like depigmentation has been observed following immunotherapy of melanoma[6,7]. Melanins are colloidal pigments, known to have a high affinity for metal ions; therefore, certain metal ions such as zinc was found in high levels in pigmented tissues involved in melanin synthesis. As melanocyte degeneration was greater in active vitiligo, so there should be decreased zinc in pigment tissues with their defective share in melanin synthesis. Melanogenesis is a complex process with different stages. When disturbed, it may determine different types of pigmentation defects, which are classified as hypo or hyperpigmentation. The understanding of the mechanisms of melanogenesis helps us to explain the pigmentation defects observed in genodermatoses

Zinc a-2-glycoprotein (ZAG), a plasma glycoprotein is a member of the immunoglobulin gene super family and has a three-dimensional structure that is highly homologous to major histocompatibility complex class I and II molecules.[8,9] ZAG regulates melanin production by normal and malignant melanocytes. B-16 recombinant human ZAG tumors have decreased levels of tyrosinase protein and minimal tyrosinase activity.[8] Tyrosinase is a major antigen presented to the immune system on the surface of melanocytes and melanoma cells by HLA class I molecules, principally *HLA-A**0201, which itself is a major genaralised vitiligo risk allele. Indeed, *HLA-A**0201 and

TYR 402Arg exhibit significant genetic interaction in promoting genaralised vitiligo susceptibility [5], reflecting a corresponding biological interaction. Tyrosinase is an important signal by which the immune system recognizes melanocytes, and tyrosinase-402Arg is likely to make a greater contribution than tyrosinase-402Gly to immune surveillance (and thus protection) against malignant melanoma and to susceptibility to genaralised vitiligo.

MATERIALS AND METHODS

This study was conducted for a period of one year from may 2016 to may 2017. 35 diagnosed patients of vitiligo who attended the dermatology OPD of various hospitals in Karimnagar were included in the study. Patients who were not on any treatment with zinc in the four weeks prior to diagnosis were included in the study group. A detailed cutaneous and systemic examination was done in all patients and patients with other skin disorders or systemic diseases were excluded from the study group. The control group included normal volunteers who were not on zinc medication in any form. 3 ml of fasting blood was collected in clot activator coated sterile tubes (JKvial) and was centrifuged for 10 minutes at 1500-2000 rpm. Coral kit was used to measure serum zinc levels on CPC-semi auto analyser.

Normal range of serum zinc level is 60-120 µg/dl.

RESULTS

The average serum levels of zinc in vitiligo patients and controls are presented in **Table 1.** The serum zinc level in controls ranged from 60 to 120 µg/dl with a mean value of 85.29±11.16 µg/dl. The serum zinc level in vitiligo patients ranged from 30.10 to 120 µg/dl, with a mean value of 35.54 ±11.10 µg/dl (Table 1). Unpaired t-test results showed that there is a significant difference between the zinc serum level in patients with vitiligo compared with healthy subjects (p = <0.0001*).

Table 1: Mean serum zinc level in vitiligo patients and controls

Study subjects	Serum zinc [µg/dl]	P-value
Mean ± SD		
Vitiligo group (N = 35)	35.54 ±11.10	<0.0001*
Control group (N = 35)	81.29 ±11.32	

DISCUSSION

Zinc, as a trace element, has many vital functions in human. It is anti apoptotic factor and needed as a cofactor for antioxidant defense system. It plays an important role in the process of melanogenesis. It may be effective in prevention and treatment of vitiligo.

Zinc deficiency impairs growth and development, decreases the resistance to local infection, delays wound healing, may produce hyperkeratotic skin lesions, apathy, depression, behavioral changes, and taste disturbances. Conditioned zinc deficiency occurs with the formation of insoluble complexes with calcium, fiber and phytate thus markedly decreasing the intestinal absorption of zinc. Decrease in plasma levels of zinc may occur in a woman on oral contraceptives, in pregnancy, cirrhosis of liver, viral hepatitis, parasitic infestations, acute infections, neoplastic conditions and myocardial infarction. Zinc deficient states were associated with steatorrhea, renal failure, severe burns and mongolism. Alcohol consumption may increase the urinary zinc levels.[10,11,12]

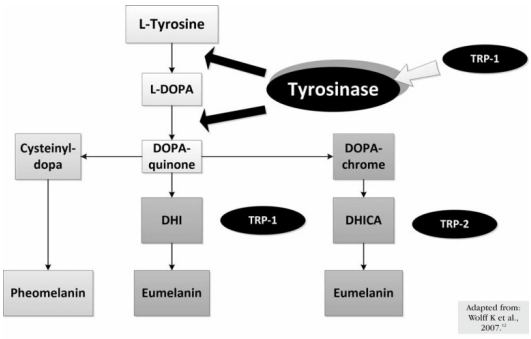
Research at the molecular level has demonstrated deficiency of antioxidant substances in vitiliginous skin. This leads to cytotoxic action of reactive oxygen species such as superoxide anion and hydroxyl radical which are generated by the ultraviolet damaged epidermis. The free radicals are also cytotoxic to melanocytes and inhibit tyrosinase.[11] Essentiality of zinc is related mainly to its function as the metal moiety of important enzymes. Zinc is considered as an antioxidant because the extracellular enzyme superoxide dismutase is zinc-dependent. It plays a vital role in the protection against free radical damage. Zinc as a trace element, plays an important role in the process of melanogenesis. Trace elements including zinc catalyze the rearrangement of dopachrome to form 5,6 - dihydroxy indole - 2 carboxylic acid (DHICA) in the process of melanogenesis.[12] Two proteins similar to tyrosinase (40% homologous amino acids), tyrosinase-related protein-1 (TRP-1) and tyrosinase-related protein-2 (TRP-2), are also present in the membrane of melanosomes.

Although its precise role is not yet clarified, it is possible that TRP-1 has a role in the activation and stabilization of tyrosinase, melanosome synthesis, increased eumelanin/ pheomelanin ratio and a role against oxidative stress due to its peroxidase effect (Figure 1).[13,14] The results found by Jimbow et al. suggest that the premature death of melanocytes in Vitiligo is related to an increased sensitivity to oxidative stress caused by changes in TRP-1.[16] TRP-2 acts as a dopacrome tautomerase and, similarly to tyrosinase, requires a metal ion for its activity, zinc instead of copper.[13,14,15] Figure 1 shows the synthesis of the two types of melanin and the functions of the major enzymes involved. zinc is the abundant trace element of melanosomes (e.g. its concentration in human hair melanosomes is the highest Zn concentration attained in a structural element of human body), the next question striking mind is where and why it is localized in these organelles. Zinc-melanin and zinc-protein interactions can be expected to occur in melanosomes. What is the distribution of zinc between melanin and protein moieties of melanosomes has not been clearly defined because only a few studies have addressed the cardinal question of zinc distribution within melanosomes. In

order to understand the function of metals in living systems, knowledge is needed on the biochemical basis of metal interactions with intracellular targets. The balance between essentiality and toxicity of metals can be regulated by specific binding sites for metals and hence knowledge concerning intracellular biochemical speciation is of importance.

Melanin behaves as a natural cation exchange material and is therefore able to incorporate various ions both in vitro and in vivo . Melanin pigments in melanosomes in vivo are always associated with a protein moiety which can also influence metal ion - melanin interactions. Among various metals only zinc was found in a higher amount in the melanin-human albumin-Zn complexes. Melanin pigments in melanosomes in vivo are always associated with a protein moiety which can also influence metal ion - melanin interactions.

Figure1: Showing synthesis of melanin



CONCLUSION

Melanocytes are responsible for the cutaneous synthesis and distribution of melanin, an essential pigment for photoprotection. This process, which is called melanogenesis, involves different stages, from melanocyte embryogenesis to melanosome transfer to neighboring keratinocytes. The importance of each of these stages and their mechanisms is evident in clinical genetic defects (genodermatoses with depigmentation or hypopigmentation).

In the present study it has been proved that serum Zinc level is very low in Vitiligo patients compared to healthy controls. It signifies the role of Zinc in the pathogenesis of Vitiligo. Large scale studies are needed to confirm the above findings and assess the effect of oral Zinc supplements in those patients with low Zinc levels.

REFERENCES

1. Kovacs SO. Vitiligo. J Am Acad Dermatol 1998;38:647-66.
2. Schallreuter KU, Wood JM, Berger J. Low catalase levels in the epidermis of patients with vitiligo. J Invest Dermatol 1991;97:1081-5.
3. Prasad AS. Zinc: An overview. Nutrition 1995;11:93-9.
4. Prota G. Progress in the Chemistry of Melanins and related metabolites. Med Res Rev 1988;8:525-56.
5. Spritz RA. The genetics of generalized vitiligo. Curr Dir Autoimmune. 2008;10:244–57.
6. Manolache L, Benea V. Stress in patients with alopecia areata and vitiligo. J Eur Acad Dermatol Venereol. 2007;21:921–8.
7. Lebwohl MG, Heymann WR, Berth-Jones J, Coulson I. 2nd ed. Philadelphia: Mosby Elsevier; 2006. Treatment of skin disease. Comprehensive Therapeutic Strategies; pp. 683–687.
8. Hale LP. Zinc a-2-glycoprotein regulates melanin production by normal and malignant melanocytes. J Invest Dermatol. 2002;119:464–70.
9. Anchez LM, Chirino AJ, Bjorkman PJ. Crystal structure of human ZAG: A fat-depleting factor related to MHC molecules. Science. 1999;283:1914–9.
10. Namazi MR. Phnytoin as a novel anti-vitiligo weapon. J Autoimmune Dis. 2005;2:11.
11. Mandelcorn-Monson RL, Shear NH, Yau E, Sambhara S, Barber BH, Spaner D, et al. Cytotoxic T lymphocyte reactivity to gp100, melan A/MART I, and tyrosinase, in HLA-A2-positive vitiligo patients. J Invest Dermatol. 2003;121:550–6.
12. Yaghoobi R, Omidian M, Bagherani N. Vitiligo: A review of the published work 2011;38:419-31. J Dermatol. 2011;38:419–31.
13. Park HY, Kosmadaki M, Yaar M, Gilchrest BA. Cellular mechanisms regulating human melanogenesis. Cell Mol Life Sci. 2009;66:1493–506.
14. Schallreuter KU, Kothari S, Chavan B, Spencer JD. Regulation of melanogenesis-- controversies and new concepts. ExpDermatol. 2008;17:395–404.
15. Slominski A, Tobin DJ, Shibahara S, Wortsman J. Melanin pigmentation in mammalian skin and its hormonal regulation. PhysiolRev. 2004;84:1155–228.
16. Jimbow K, Chen H, Park JS, Thomas PD. Increased sensitivity of melanocytes to oxidative stress and abnormal expression of tyrosinase-related protein in vitiligo. Br J Dermatol. 2001;144:55–65.

How to cite this article : Venugopal B, Kishan Reddy H. Study of serum Zinc levels in patients with vitiligo of north Telangana. Perspectives in Medical Research 2018;6(1):34-36.

Sources of Support: Nil,Conflict of interest:None declared